# REACTIONS OF 6-METHYL-2-PYRIDONE

BY

ANTHONY WOLFGANG SCHRECKER

Doktorandum, University of Vienna, 1937
Licencié-ès-Sciences, Sorbonne (Paris), 1940

## AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1948

URBANA, ILLINOIS
1948

# REACTIONS OF 6-METHYL-2-PYRIDONE

BY

ANTHONY WOLFGANG SCHRECKER

Doktorandum, University of Vienna, 1937
Licencié-ès-Sciences, Sorbonne (Paris), 1940

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1948

URBANA, ILLINOIS
1948

ACKNOWLEDGMENT

The author wishes to express his grateful appreciation to Professor Roger Adams for his suggestion of this problem and for his encouragement and guidance during the course of this investigation.

R. UNIV.
BIBLIOTHEEK
LEIDEN

# REACTIONS OF 6-METHYL-2-PYRIDONE

## Introduction

The known activity of the methyl group in 2-picoline and similar compounds has been attributed to the double bond between the nitrogen and the carbon carrying the methyl group (1). Consideration of the formula of such compounds as 1,6-dimethyl-2-pyridone does not show this double bond unless they are resonance hybrids of a cyclic amide and a betaine form (2). It was therefore found desirable to test the behavior of 1,6-dimethyl-2-pyridone, its isomer carrying a methyl group in the 4-position and various related compounds in the presence of reagents, especially carbonyl compounds, which undergo condensation reactions with active methyl groups.

Another reason for undertaking this investigation was the desire to arrive at compounds which could serve as starting materials for a synthesis of the alkaloid cytisine (3), a compound which contains a 2-pyridone nucleus with a six-membered ring linking the nitrogen and carbon 6.

## Discussion Of Results

1,6-Dimethyl-2-pyridone was prepared from 6-methyl-2-pyridone sodium and dimethyl sulfate and its structure proven conclusively by characterization of derivatives and chemical degradation experiments. The synthesis of 1,4-dimethyl-2-pyridone was also accomplished.

Condensation of 1,6-dimethyl-2-pyridone with *m*-nitrobenzaldehyde produced the styryl derivative in low yield. With formaldehyde in the presence of piperidine a high-melting condensation product was formed, the structure of which was not determined. With chloral only an addition compound could be obtained.

A more satisfactory method for the preparation of styryl-

pyridones was found to be the condensation of 2-acetamido-6 (and 4-)-methylpyridine with benzaldehyde, followed by hydrolysis of the acetyl group and treatment with sodium nitrite in sulfuric acid.

The condensation of 1,6-dimethyl-2-pyridone with ethyl oxalate in the presence of ethoxide ion was found to proceed readily to produce ethyl 1-methyl-2-pyridone-6-pyruvate in excellent yield. An electronic mechanism for this reaction has been proposed. The condensation of 1,4-dimethyl-2-pyridone with ethyl oxalate also was successful, though the yield was somewhat lower. A similar reaction had been carried out previously with 1,4-dimethylcarbostyril (4). The pyruvic esters were hydrolyzed to the corresponding acids which were made to undergo oxidative decarboxylation to yield 1-methyl-2-pyridone-6-acetic and 4-acetic acid respectively. This reaction was carried out with hydrogen peroxide in the presence of excess base; when however the potassium salt of the 6-pyruvic ester was treated with hydrogen peroxide in the absence of excess base, 1-methyl-2-pyridone-6-carboxylic acid, previously described (5), was formed.

In attempts to arrive at pyridocoline derivatives suitable for a cytisine synthesis, 6-methyl-2-pyridone-N-propionitrile and N-propionic acid were prepared by application of a known method (6) and the corresponding ester treated with base catalysts, but no internal condensation with the 6-methyl group took place. 6-Methyl-2-pyridone-N-acetic ester was prepared and treated with ethyl oxalate; only one of the carbethoxy groups of the oxalic ester underwent condensation and no ring closure occurred.

The theory that N-alkylpyridones are resonance hybrids of an amide and a betaine structure permits to predict that an N-alkyl-2-pyridone-6-acetic ester is similar in its reactivity to acetoacetic ester and the corresponding nitrile to cyanoacetic ester. This was confirmed by preparing ethyl 1-methyl-2-pyridone-6-acetate from the 6-acetic acid and the 6-acetonitrile from the 6-pyruvic via the $\alpha$-oximino acid, then

subjecting these compounds to condensation reactions in the presence of base catalysts. While no reaction occurred with esters, it took place with alkyl and acyl halides.

Thus 1-methyl-6-phenethyl-2-pyridone was prepared by condensation of the 6-acetate and 6-acetonitrile with benzyl chloride, followed by hydrolysis and decarboxylation. 6-*n*-Amyl-1-methyl-2-pyridone and 6-acetonyl-1-methyl-2-pyridone were prepared from the 6-acetate by an analogous method involving the use of *n*-butyl halide and of acetyl chloride. The 6-acetonitrile, but not the 6-acetate, also underwent condensation with benzaldehyde in the presence of piperidine.

The condensation of 6-methyl-2-pyridone sodium with γ-phenoxypropyl bromide was carried out. Both the N-alkyl-pyridone, which might serve as an intermediate for the synthesis of a substituted pyridocoline, and the pyridyl ether were obtained and their structures proven by examination of their infrared absorption spectra.

## BIBLIOGRAPHY

1. Mills and Smith, *J. Chem. Soc.*, **121**, 2724 (1922).
2. Arndt and Kalischek, *Ber.*, **63**, 587 (1930).
3. Späth and Galinovsky, *ibid.*, **66**, 1338 (1933).
4. Kaslow and Cook, *J. Am. Chem. Soc.*, **67**, 1969 (1945).
5. Späth and Koller, *Ber.*, **56**, 880 (1923).
6. Adams and Jones, *J. Am. Chem. Soc.*, **69**, 1803 (1947).

## VITA

The author was born in Vienna, Austria on February 15, 1915. He attended a number of elementary and secondary schools and was graduated from the Bundes-Realgymnasium in Vienna I. in March, 1934. He entered the University of Vienna in April of the same year and attended it until March, 1938. He passed the Doktorandum in October, 1937. In April, 1938 he entered the Sorbonne in Paris, from which he received the degree of Licencié-ès-sciences in June, 1940. After working for several months at the University of Toulouse, France, he came to the United States in October, 1942. He was employed as a chemist by the Polychemical Company in New York, N. Y. from December, 1942 until January, 1943 and by the May Chemical Corporation in Newark, N. J. from February, 1943 until January, 1944, and as a technical adviser by the French Supply Council in Washington, D. C. from January, 1944 until August, 1946. In September, 1946 he entered the Graduate College of the University of Illinois. He held an Assistantship in Chemistry from September, 1946 until the following January and the Standard Oil Company (Indiana) Fellowship from September, 1947 through June, 1948.

Digitized by the Internet Archive
in 2026

https://archive.org/details/IA41549807_0027